Notice of Allowability

Application No.	Applicant(s)
09/845,129	Duff
Examiner	**Art Unit**
Arun Chakrabarti	1634

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *7/8/03*.

2. ☒ The allowed claim(s) is/are *1-6, 8-20, 29-40, and 58-66*.

3. ☒ The drawings filed on *Apr 27, 2001* are accepted by the Examiner.

4. ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

   a) ☒ All b) ☐ Some* c) ☐ None of the:

   1. ☒ Certified copies of the priority documents have been received.
   2. ☒ Certified copies of the priority documents have been received in Application No. *09/845,129*.
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   *Certified copies not received: _____.

5. ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

   (a) ☐ The translation of the foreign language provisional application has been received.

6. ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS must be submitted.

   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached

   1) ☐ hereto or 2) ☐ to Paper No. _____.

   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the examiner.

   (c) ☐ including changes required by the attached Examiner's Amendment/Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1 ☐ Notice of References Cited (PTO-892)
2 ☐ Notice of Informal Patent Application (PTO-152)
3 ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
4 ☒ Interview Summary (PTO-413), Paper No. *0803*.
5 ☐ Information Disclosure Statement(s) (PTO-1449), Paper No(s). _____
6 ☐ Examiner's Amendment/Comment
7 ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
8 ☐ Examiner's Statement of Reasons for Allowance
9 ☐ Other

Arun kr. Chakrabarti

CLAIMSPTO/N.O.A.

C. DESSAU

08/26/03

1. (Currently Amended) A method for detecting whether a subject ~~has~~ is suffering from or is predisposed to developing a disease or condition ~~that is~~ associated with an IL-1 inflammatory haplotype, comprising detecting ~~a plurality of~~ one or more alleles ~~from an IL-1 inflammatory haplotype~~ selected from the group consisting of: ~~an IL-1 44112332 inflammatory haplotype, and an IL-1 33441461 inflammatory haplotype~~ allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, wherein the presence of ~~the plurality of~~ said one or more alleles indicates that the subject is predisposed to the development of or has the disease or condition.

2. (Original) A method of claim 1, wherein the disease of condition is selected from the group consisting of an inflammatory disease, a degenerative disease an immunological disorder, an infectious disease, a trauma induced disease, and a cancer.

3. (Original) A method of claim 1, wherein said detecting step is selected from the group consisting of:

   a) allele specific oligonucleotide hybridization;
   b) size analysis;
   c) sequencing;
   d) hybridization;
   e) 5' nuclease digestion;
   f) single-stranded conformation polymorphism;
   g) allele specific hybridization;
   h) primer specific extension; and
   j) oligonucleotide ligation assay.

4. (Original) A method of claim 1, wherein prior to or in conjunction with detection, the nucleic acid sample is subject to an amplification step.

5. (Original) A method of claim 4, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID Nos.8-32.

6. (Original) A method of claim 3, wherein said size analysis is preceded by a restriction enzyme digestion.

8. (Currently Amended) A method for selecting an appropriate therapeutic for an individual that ~~has~~ is suffering from or is predisposed to developing a disease or disorder ~~that is~~ associated with an IL-1 polymorphism, comprising the steps of: detecting ~~a plurality of~~ one or more alleles ~~from an IL-1 inflammatory haplotype~~ selected from the group consisting of: ~~an IL-1 44112332 inflammatory haplotype, and an IL-1 33441461 inflammatory haplotype~~ allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 alleles.

9. (Original) A method of claim 8, wherein said detecting is performed using a technique selected from the group consisting of:

a) allele specific oligonucleotide hybridization;
b) size analysis;
c) sequencing;
d) hybridization;
e) 5' nuclease digestion;
f) single-stranded conformation polymorphism;
g) allele specific hybridization;
h) primer specific extension; and

j) oligonucleotide ligation assay.

10. (Original) A method of claim 8, wherein prior to or in conjunction with detecting, the nucleic acid sample is subjected to an amplification step.

11. (Original) A method of claim 10, wherein said amplification step employs a primer selected from the group consisting of SEQ ID Nos. 8-32.

12. (Original) A method of claim 9, wherein said size analysis is preceded by a restriction enzyme digestion.

13. (Currently Amended) A method of claim 9, wherein the disease or condition is selected from the group consisting of: an inflammatory disease, a degenerative disease an immunological disorder, an infectious disease, a trauma induced disease, and a cancer.

14. (Original) A method of claim 9, wherein the therapeutic is a modulator of an IL-1 activity.

15. (Original) A method of claim 14, wherein the IL-1 activity is IL-1α.

16. (Original) A method of claim 14, wherein the IL-1 activity is IL-1β.

17. (Original) A method of claim 14, wherein the IL-1 activity is IL-1RN.

18. (Original) A method of claim 14, wherein the modulator of an IL-1 activity is a protein, peptide, peptidomimetic, small molecule, nucleic acid or a nutraceutical.

19. (Original) A method of claim 14, wherein the modulator is an agonist.

20. (Original) A method of claim 14, wherein the modulator is an antagonist.

29. (Currently Amended) A method for treating or preventing the development of a disease or condition ~~that is~~ associated with an IL-1 polymorphism in a subject comprising the steps of: detecting ~~a plurality of~~ one or more alleles ~~from an IL-1 inflammatory haplotype~~ selected from the group consisting of: ~~an IL-1 44112332 inflammatory haplotype, and an IL-1 33441461 inflammatory haplotype~~ allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN; and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 inflammatory haplotype.

30. (Original) A method of claim 29, wherein the detecting step is selected from the group consisting of:

a) allele specific oligonucleotide hybridization;
b) size analysis;
c) sequencing;
d) hybridization;
e) 5' nuclease digestion;
f) single-stranded conformation polymorphism;
g) allele specific hybridization;
h) primer specific extension; and
j) oligonucleotide ligation assay.

31. (Original) A method of claim 29, wherein prior to or in conjunction with detecting, the nucleic acid sample is subjected to an amplification step.

32. (Original) A method of claim 29, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID Nos. 8-32.

33. (Original) A method of claim 30, wherein said size analysis is preceded by a restriction enzyme digestion.

34. (Original) A method of claim 30, wherein the therapeutic is selected from the group consisting of: a modulator of an IL-1 activity.

35. (Original) A method of claim 34, wherein the IL-1 activity is IL-1α.

36. (Original) A method of claim 34, wherein the IL-1 activity is IL-1β.

37. (Original) A method of claim 34, wherein the IL-1 activity is IL-1Ra.

38. (Original) A method of claim 34, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.

39. (Original) A method of claim 34, wherein the modulator is an agonist.

40. (Original) A method of claim 34, wherein the modulator is an antagonist.

58. (New) The method of claim 1, further comprising detecting allele 2 of the VNTR marker of IL-1RN.

59. (New) The method of claim 8, further comprising detecting allele 2 of the VNTR marker of IL-1RN.

60. (New) The method of claim 29, further comprising detecting allele 2 of the VNTR marker of IL-1RN.

61. (New) A method for detecting whether a subject is suffering from or is predisposed to developing a cardiovascular disease, comprising detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, wherein the presence of said one or more alleles indicates that the subject is predisposed to the development of or has a cardiovascular disease.

62. (New) A method for detecting whether a subject is suffering from or is predisposed to developing osteoporosis, comprising detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, wherein the presence of said one or more alleles indicates that the subject is predisposed to the development of or has osteoporosis.

63. (New) A method for selecting an appropriate therapeutic for an individual that is suffering from or is predisposed to developing a cardiovascular disease, comprising the steps of: detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 alleles.

64. (New) A method for selecting an appropriate therapeutic for an individual that is suffering from or is predisposed to developing osteoporosis, comprising the steps of: detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN, and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 alleles.

65. (New) A method for treating or preventing the development of a cardiovascular disease in a subject comprising the steps of: detecting one or more alleles selected from the group

consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN; and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 inflammatory haplotype.

66. (New) A method for treating or preventing the development of osteoporosis in a subject comprising the steps of: detecting one or more alleles selected from the group consisting of: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 2 of the -511 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 1 of the VNTR marker of IL-1RN; and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 inflammatory haplotype.